



DEPARTMENT OF THE AIR FORCE  
59TH MEDICAL WING (AETC)  
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

6 MAY 2016

MEMORANDUM FOR ST

ATTN: SHARON LAWSON

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Hyperbaric Normothermic Perfusion Mitigates Reperfusion Injury in Porcine VCA** presented at/published to **Association of Surgeons Great Britain and Ireland 11-13 May 2016** with MDWI 41-108, and has been assigned local file **#16191**.
2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.
3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.
4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC  
Director, Clinical Investigations & Research Support

## PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

### INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
  - a. In Section 2, add the funding source for your study [ e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]
  - b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.
2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.
3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.
4. Attach a copy of your abstract, paper, poster and other supporting documentation.
5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.
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  - a. Print their name, rank/grade, title; sign and date the form in the approving authority's signature block or use an electronic signature.
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9. Once your manuscript, poster or presentation has been approved for a one-time public release, you may proceed with your publication or presentation submission activities, as stated on this form. **Note:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.
10. If your manuscript is accepted for scientific publication, please contact the 59 CRD/Publications and Presentations Section at 292-7141. This information is reported to the 59 MDW/CC. All medical research or technical information publications/presentations must be reported to the Defense Technical Information Center (DTIC). See 59 MDWI 41-108, *Presentation and Publication of Medical and Technical Papers*, for additional information.

**NOTE:** All abstracts, papers, posters, etc., should contain the following disclaimer statement:

*"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"*


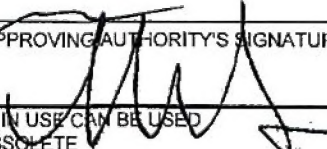
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*"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02\_AFI 40-402."*

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PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS			
1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol) Sharon Lawson, CTR, 59MDW ST	3. GME/GHSE STUDENT: <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	4. PROTOCOL NUMBER: FWH20150008A
5. PROTOCOL TITLE: (NOTE: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.) Evaluation of Tissue Preservation Method and Device for 8 hours for Gracilis Myocutaneous Flap Transplant in a Swine model (Sus scrofa d)			
6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED: Hyperbaric normothermic perfusion mitigates reperfusion injury in porcine VCA			
7. FUNDING RECEIVED FOR THIS STUDY? <input type="checkbox"/> YES <input type="checkbox"/> NO FUNDING SOURCE: AFMSA/59 MDW ST			
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13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email) Corpus Raul S, raul.s.corpus.ctr@mail.mil			14. DUTY PHONE/PAGER NUMBER 2105394404
15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.			
LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
a. Primary/Corresponding Author Sharon Lawson	CTR	59MDW ST RESTOR	
b. Lin Wang	O-3	59MDW ST RESTOR	
c. Renford Cindass	O-3	59MDW ST RESTOR	
d. Kevin Wu	CTR	59MDW ST RESTOR	
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16. AUTHOR'S PRINTED NAME, RANK, GRADE Sharon Lawson, CTR		17. AUTHOR'S SIGNATURE 	18. DATE April 26, 2016
19. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE Michael R Davis, Lt Col, Director-RESTOR, Deputy Commander		20. APPROVING AUTHORITY'S SIGNATURE 	21. DATE April 26, 2016

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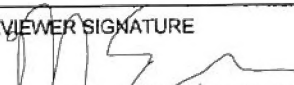
## **1st ENDORSEMENT (59 MDW/SGVU Use Only)**

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# Hyperbaric normothermic perfusion mitigates reperfusion injury in porcine VCA

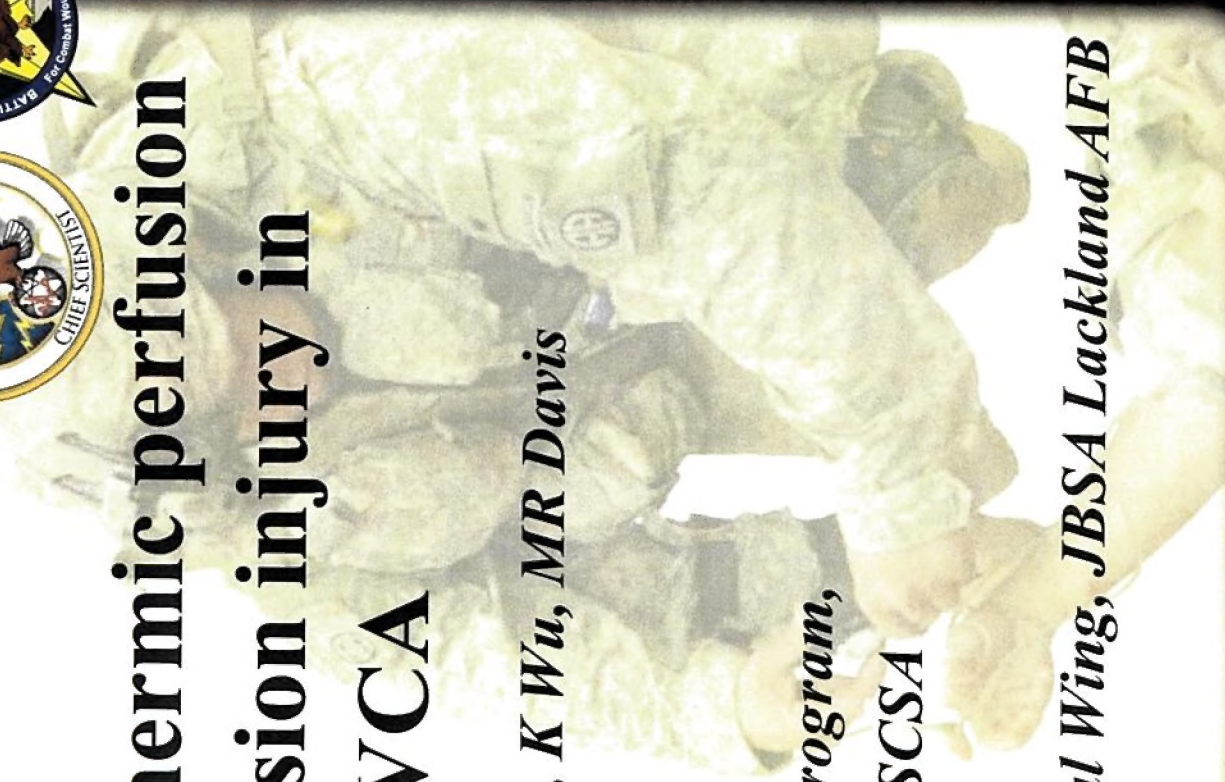
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# Disclaimer

The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of Defense.

The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended





## Background

- **Vascularized Composite Allotransplantation can reconstruct any non-visceral tissue defect**
- **VCA is a clinical reality for military trauma patients**





## Background

- **The requirement for long term systemic immunosuppression limits it's application to only a few highly motivated patients**
- **Treatment failures, morbidity and mortality associated with VCA means that it remains an experimental modality<sup>1</sup>**
- **Reconstructive surgeons are divided on the utility of VCA<sup>2</sup>**
- **Further research is mandatory before the field can move forward**

<sup>1</sup>Tullius, S., Uehara, H., Yang, X., & Edtinger, K. (2014). Current status of vascularized composite tissue allotransplantation. Burns & Trauma, 2(2), 53. doi:10.4103/2321-3868.130184

<sup>2</sup>Bertrand, A. A., Sen, S., Otake, L. R., & Lee, G. K. (2014). Changing attitudes toward hand allotransplantation among North American hand surgeons. Annals of Plastic Surgery, 72 Suppl 1, S56-60





## Ischemia-reperfusion injury (IRI)

- Exacerbation of cellular/tissue injury after an ischemic insult with re-establishment of blood flow
  - Generation of oxidative stress
  - Microvascular obstruction/thrombosis
  - Neutrophil activation
  - Complement activation
  - Release of anaphylotoxins
- Increasing severity of IRI at time of transplant in solid organs associated with increased rates and severity of acute rejection

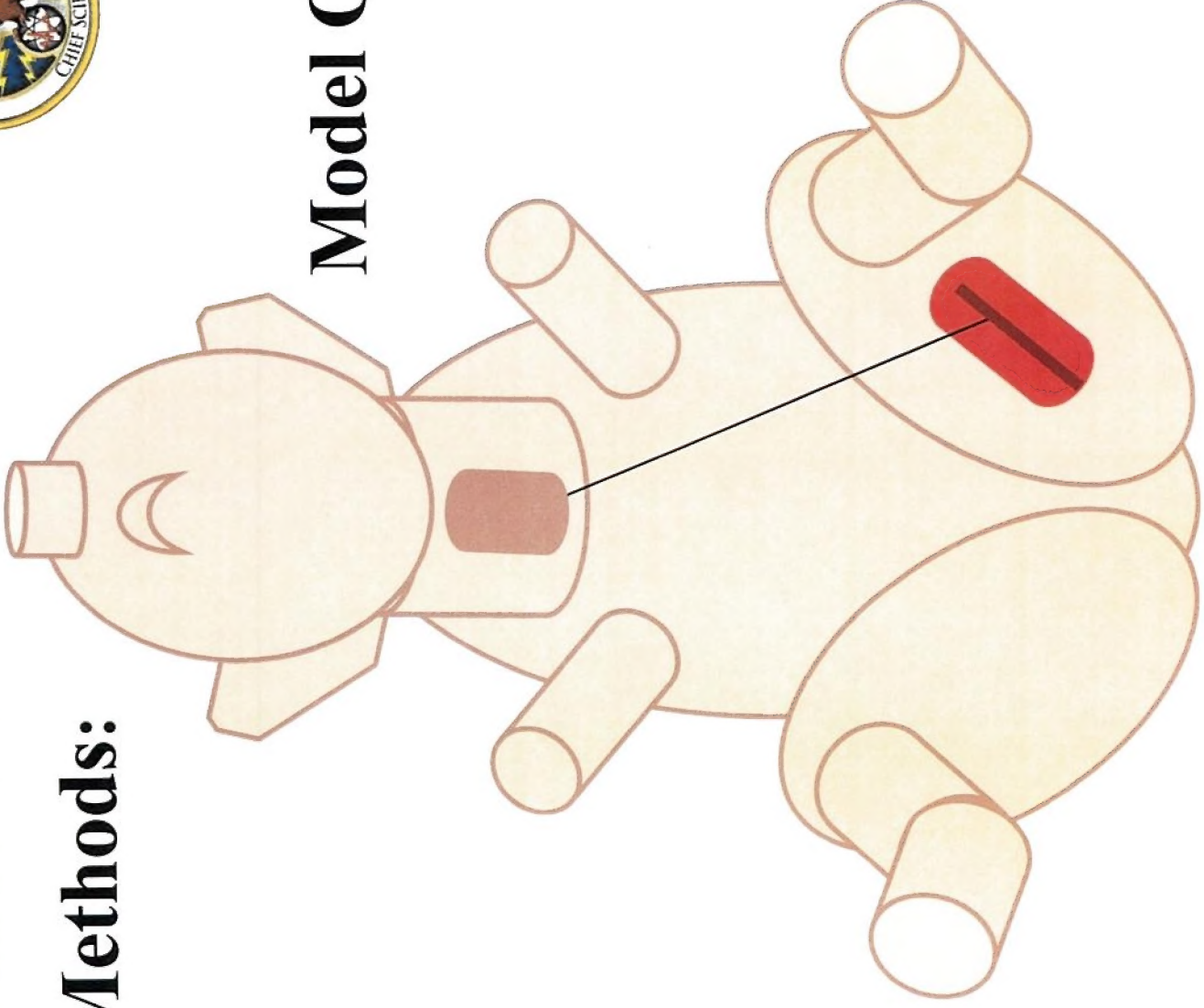
### Effects of Ischemia and Reperfusion Injury on Long-Term Graft Function

L.R. Requião-Moura, M. de Souza Durão, E.J. Tonato, A.C. Carvalho Matos, K.S. Ozaki, N.O.S. Câmara, and A. Pacheco-Silva



## Methods:

## Model Overview





# Methods



Left Hind Limb



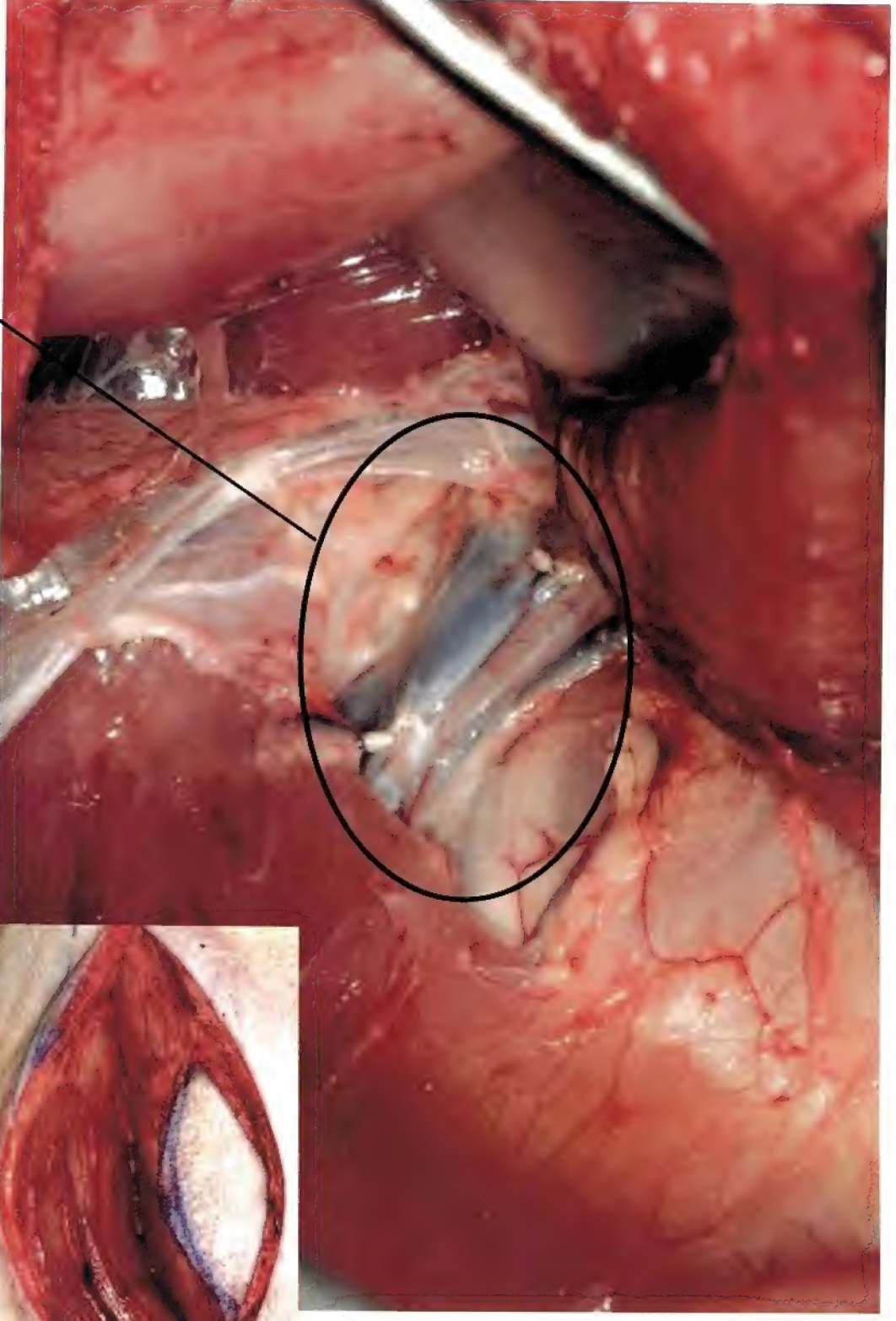
Gracilis Muscle





# Methods

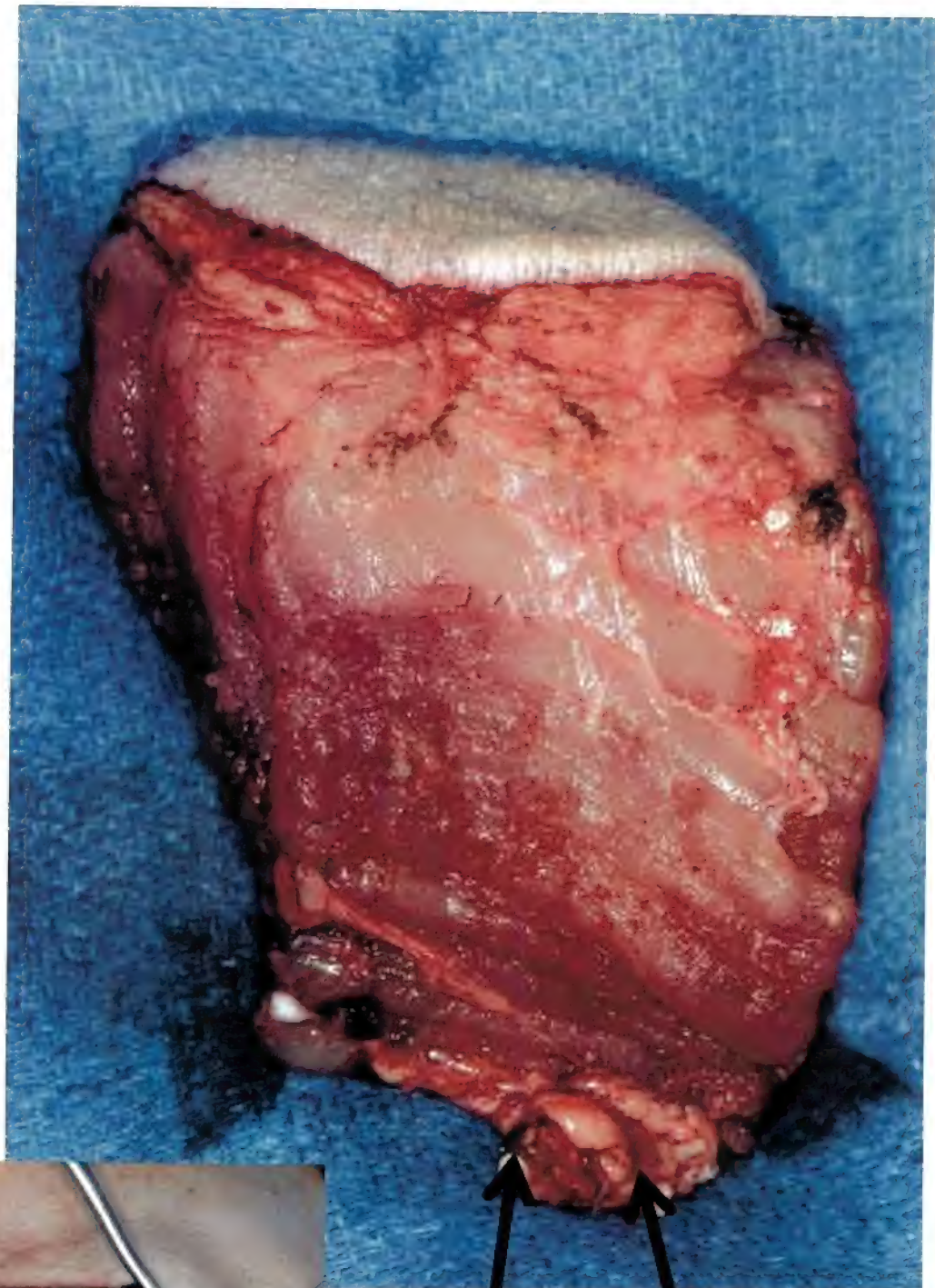
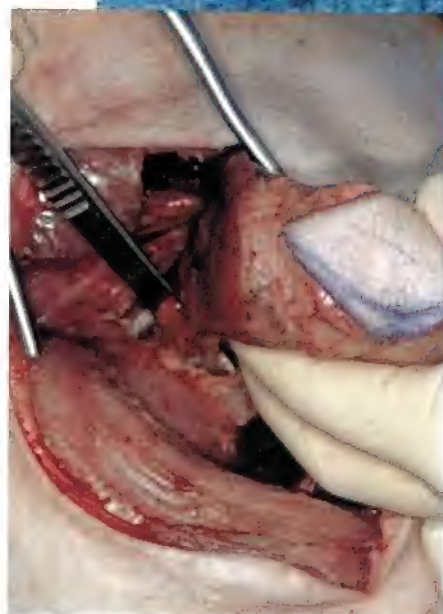
Pedicle







# Methods



Artery

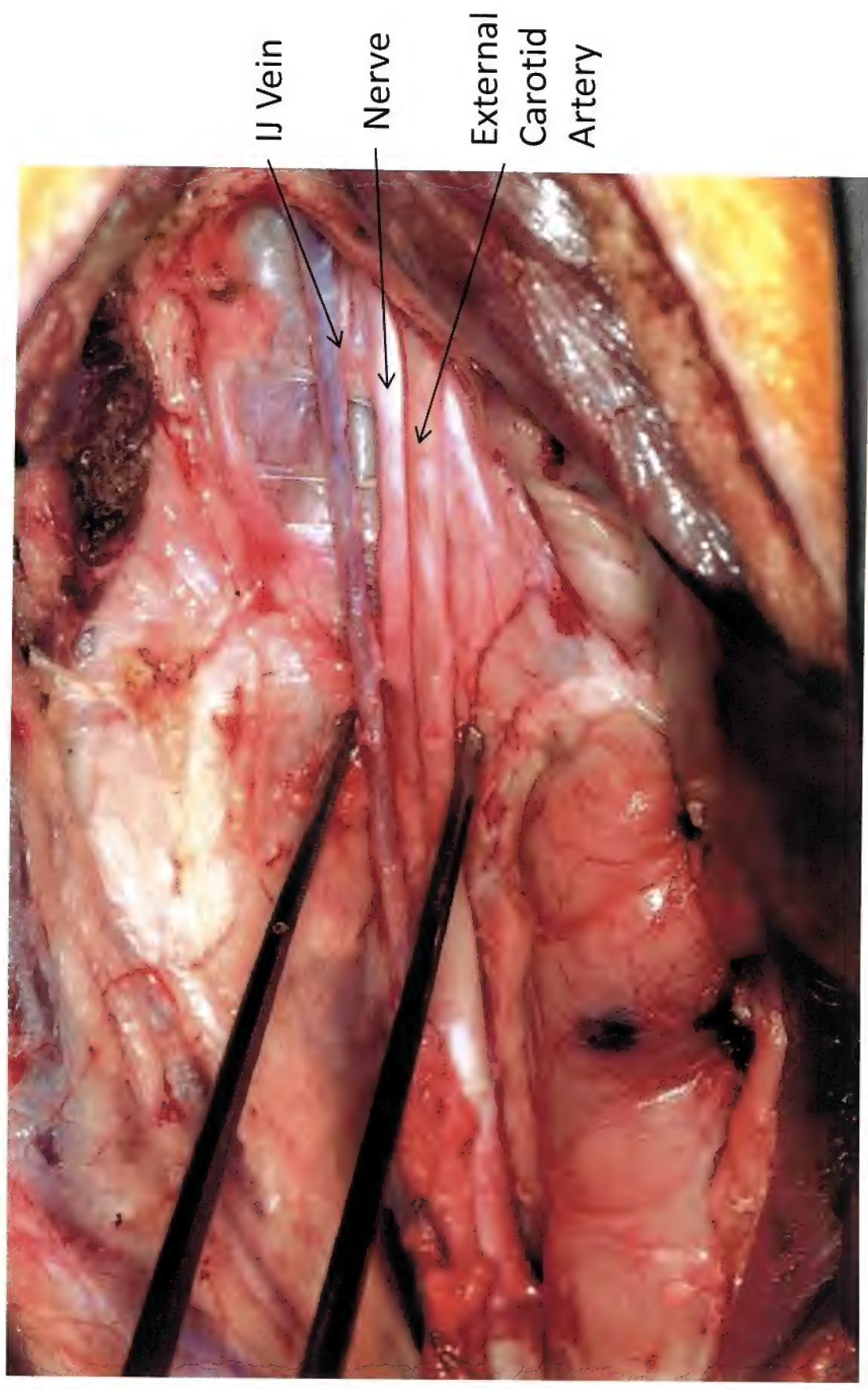
Vein





# Methods

## Exposure of Neck Vessels







## Intervention



- **Warm *ex vivo* perfusion device –**

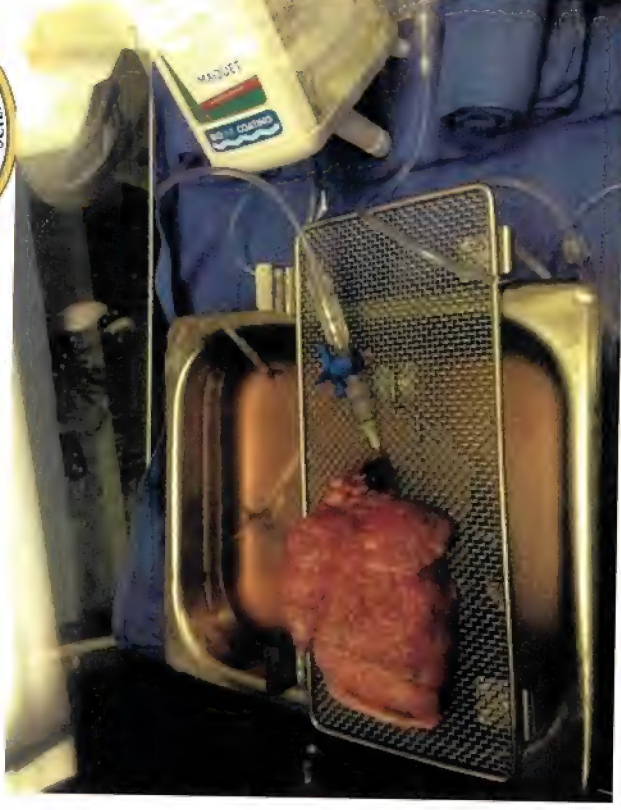
- **Experiments since the 1960s have showed ability to sustain animals with low hematocrit in hyperbaric environment**
- ***Ex vivo* perfusion of transplant organs highly desirable**

Boerema, I., Meyne, N. G., Brummelkamp, W. H., Bouma, S., Mensch, M. H., Kamermans, F., & STERN, H. M. (1960). Life without blood]. Nederlands tijdschrift voor geneeskunde, 104, 949.

D, M. A. C. M., D, E. K. M., D, X. X. P., D, D. M. K. M., Jenni, H., c, E. G. D. H., et al. (2011). Preservation of Amputated Extremities by Extracorporeal Blood Perfusion; a Feasibility Study in a Porcine Model. Journal of Surgical Research, 171(1), 291–299. doi:10.1016/j.jss.2010.01.040



## Groups



- Model development showed that 5 hours of cold ischemia was not tolerable to muscle flap (n=5)
- Control group = 3 hours cold ischemia with UW solution (n=5)
- Intervention group = 7 hours warm ischemia (37C) (n=8)

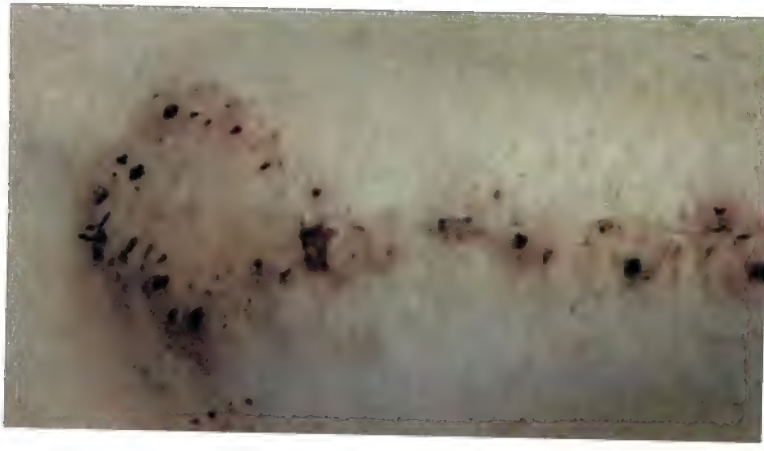




## Results

- Gracilis auto-transplants –

Treatment		
	Ctrl	Exp
Hour 0	No Muscle Necrosis	No Muscle Necrosis
Hour 3	80% with severe muscle necrosis	-----
Hour 7	-----	60% with no muscle necrosis, 40% with minimal necrosis

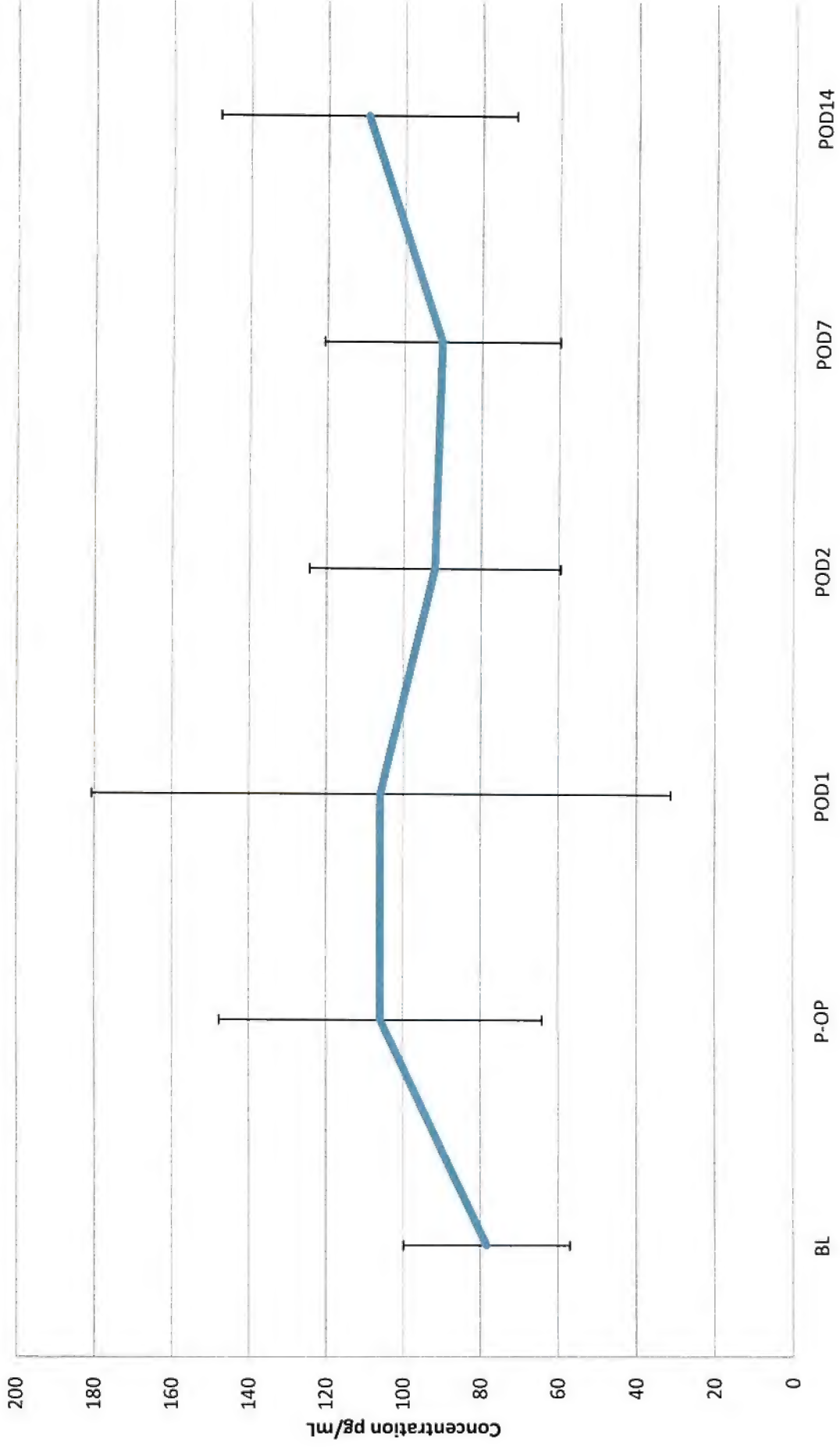




## Results



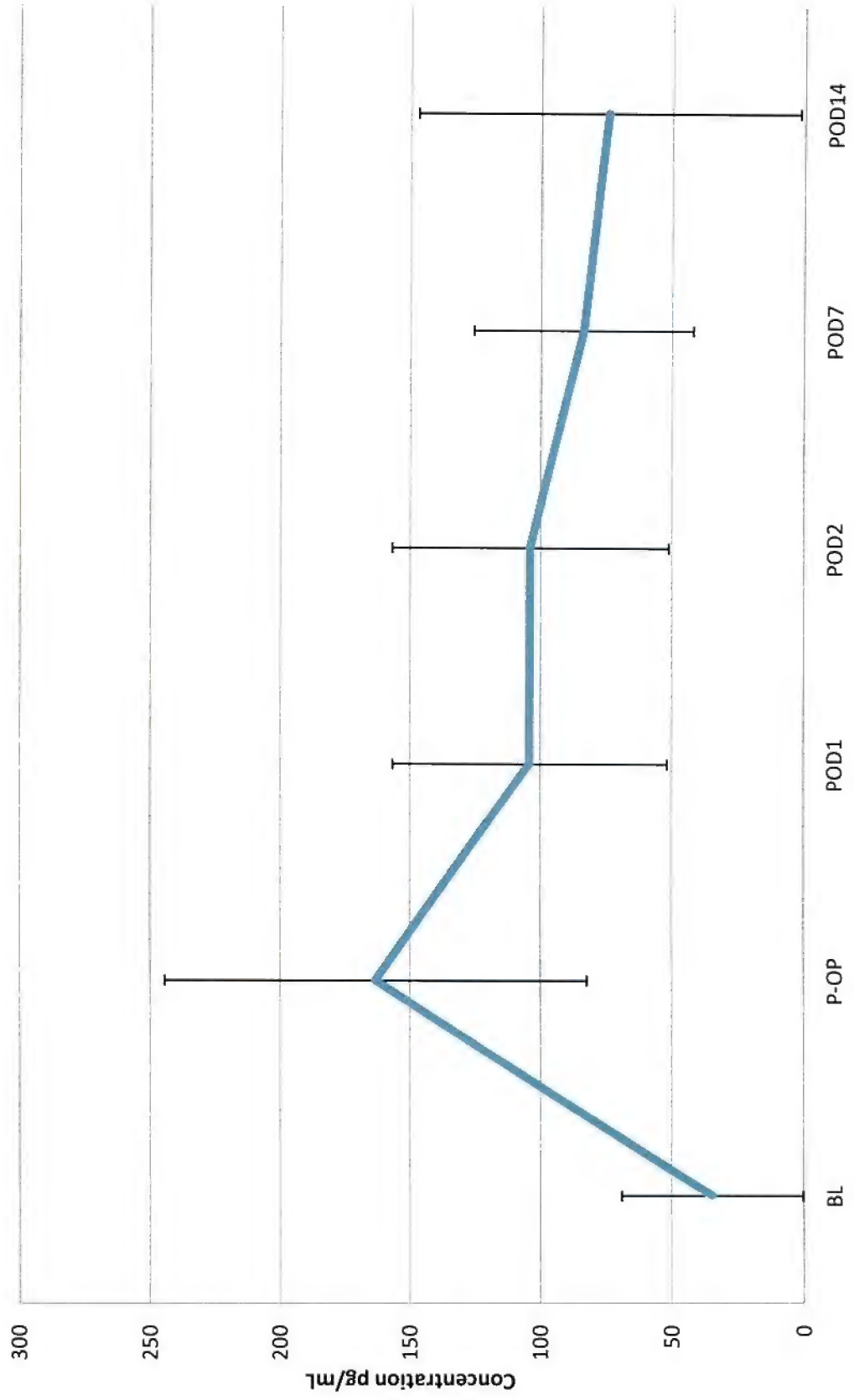
TNF-a





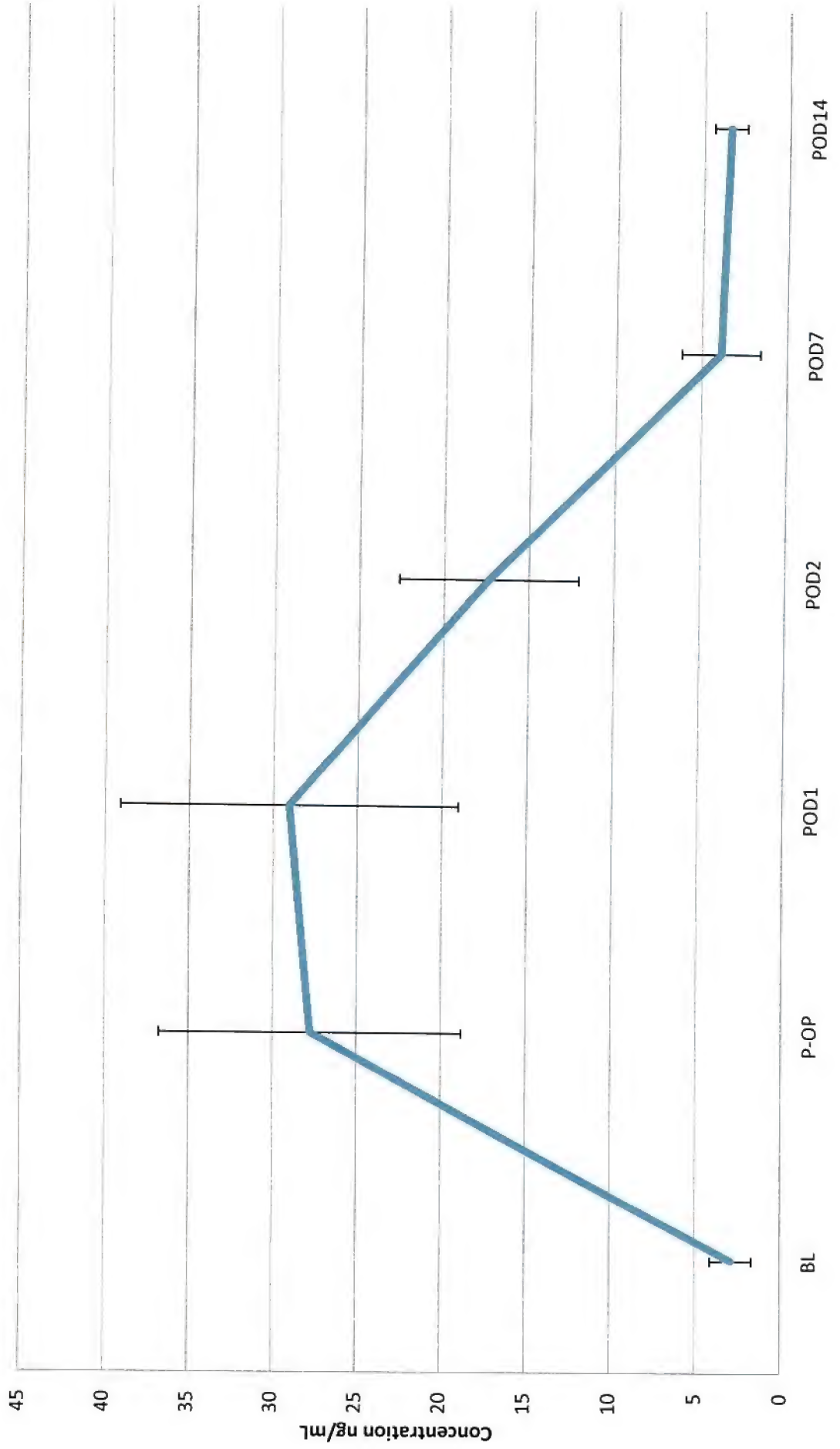


## IL-6





## Myoglobin







## Summary

- Hyperbaric normothermic perfusion reliably extends the ischemic period tolerable to tissue composites compared to the current gold standard
- Ischemic and cold-preservation injuries are mitigated
- This has application in VCA and solid organ transplantation
  - expand donor pool
  - superior matches for transplant candidates





## Future direction

- End point to be extended to 21 days to further characterize graft survival.
- Application of MSCs and combination of ischemia reperfusion agents like H<sub>2</sub>S and antioxidants as well as locally-applied graft immunosuppression in allotransplantation
- Forelimb allotransplantation







## **Acknowledgements**

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- **Raul Corpus, MPH – 59MDW Science and Technology Office**

Thank you

